

23



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,840	07/06/2001	Mark Leslie Smythe	4050.001100	8048

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EXAMINER

KAM, CHIH MIN

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/787,840

Applicant(s)

SMYTHE ET AL.

Examiner

Chih-Min Kam

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 32-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 7/6/01; 10/15/02; 10/13/04; 2/1/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION***Election/Restrictions***

1. Applicant's election without traverse of Group I, claims 1-31 and 35, in the response and amendment filed August 30, 2004 and April 15, 2005 are acknowledged. In the amendment, claims 36-38 have been cancelled. Regarding selecting one ring size (5, 6 or 7 atoms), one heteroatom or carbon in the ring structure, aromatic or cyclic alkyl structure, and one functional group for each X, Y and Z in general formula (I), applicant indicates such selections reflect sub-species as initial point for search and examination and further elect an aromatic ring of 6 carbon, X being oxygen, Z being carbonyl, and Y being a nitro group. As stated in the restriction requirement (see page 2), this selection is not a species election because each compound with different cyclic structure and functional group does not have the same special technical feature, thus is patentably distinct. Upon reconsideration, an aromatic ring of 6 carbon atoms; X being oxygen, sulfur, CH₂O- or CH₂S; Y being the group cited in claim 2 (nitro, ketone.....iodide); Z being the group cited in claim 3 (an aldehyde.....halogenated C₁₋₃alkyl group); and R₃, R₄ and R₅ being a group indicated in claim 1 for auxiliary compound will be included for examination. Therefore, claims 1-31 and 35, and the auxiliary compound having certain structure features (see above) are examined. Claims 32-34 are non-elected invention and withdrawn from consideration.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because non-dated alterations

Art Unit: 1656

have been made to the address of the inventor, Wim Denis Frans Meutermans. Applicants claim priority benefits of PCT/AU99/00812 which should be listed under 35 U.S.C. 120 instead of 119.

Informalities

The disclosure is objected to because of the following informalities:

3. The specification cites amino acid sequences (e.g., at page 8, scheme 5; page 34, line, 4, 6; and others) without indicating the sequence identifier "SEQ ID NO:". Appropriate correction is required. It appears a sequence listing for various amino acid sequences has been provided, Applicants must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) and have the sequence listing and CRF containing all the cited sequences in the specification.

Claim Objection

4. Claims 1, 11, 16 and 35 are objected to because the claim contains recitation of non-elected compounds of formula (I).
5. Claim 30 is objected to because the claim cites a misspelling word "synthesizing". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-29 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
7. Claims 1-16 and 35 are indefinite because the claims lack essential steps in the process of synthesizing a linear or cyclic peptide. The claims only recite a step of linking a cyclic aromatic

Art Unit: 1656

auxiliary compound to an amine nitrogen, there are no other steps described, e.g., how the auxiliary compound assists the formation of the peptide, and how the linear or cyclic peptide is synthesized. Claims 1 and 14 are also indefinite as to "an amine nitrogen", it is not clear which amine nitrogen the auxiliary compound links to. Claims 2-16 and 35 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

8. Claim 4 is indefinite because of the use of the term "the halogenated alkyl group is a methyl group". The term renders the claim indefinite, it is not clear how the halogenated alkyl group can be a methyl group.

9. Claim 7 recites the limitation "General Formula II" in line 2. There is insufficient antecedent basis for this limitation in the claim because there is no structure indicated. See also claims 14, 15 for General formula I, II, III or IV; claims 19, 21 and 25 for General formula III; claim 23 for General formula IV.

10. Claims 12-15, 24, 25 and 35 are indefinite because of the use of the term "difficult peptide". The term cited renders the claim indefinite, it is not clear what amino acid sequence is considered as "difficult peptide".

11. Claim 20 is indefinite because of the use of the term "if desired". The term cited renders the claim indefinite, it is not clear whether the limitation following the phrase is part of the claimed invention.

12. Claims 17-21 and 23 are indefinite because of the use of the term "a desired primary amine" or "a desired carboxylic acid". The term cited renders the claim indefinite, it is not clear which primary amine or which carboxylic acid is intended to be the desired one. Claims 18-21

Art Unit: 1656

and 23 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

13. Claim 22 is indefinite because of the use of the term "peptide fragment". The term cited renders the claim indefinite, it is not clear what sequence the peptide fragment refers to, and what peptide the fragment belongs to. Claim 22 is also indefinite as to how other peptide fragments are linked together to form a large peptide since the claim only recites the linking of first peptide fragment to the second peptide fragment.

14. Claim 26 recites the limitation " α -nitrogen of an acid residue in the desired peptide" in line 4. There is insufficient antecedent basis for this limitation in the claim, it is not clear how an acid residue can have an α -nitrogen. Claims 27-29 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

15. Claims 27 and 28 are indefinite as to "the carboxylic acid group of the C-terminal amino acid residue is replaced by a functional group", it is not clear which step (e.g., step a), b), c) or d)) the carboxylic acid is replaced?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-3, 6-8 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bodanszky (U. S. Patent 3,704,246).

Art Unit: 1656

Bodanszky teaches the amino group of an α -amino acid can react with an aromatic carbonyl compound such as 5-nitrosalicylaldehyde to form a Schiff's base, which is cyclized to form a lactone, the active lactone is then reacts with another amino acid ester and treatment with aqueous acid to remove the protecting group gives a desired peptide (column 3, line 55-column 4, line 71; claims 1-3, 6-8 and 14).

Response to Arguments

In the response to restriction requirement filed August 30, 2004, applicants argue that the U.S. Patent (3,704,246) is distinct from the claimed invention because the aromatic carbonyl compound of the patent acts as a protecting group and is not involved in formation of an amide bond, while the auxiliary compound of the claimed invention, forms a Schiff base and then undergoes reductive amination to form a single bond, followed by O-acylation and then an N-to-O acyl shift to generate the tertiary amide bond, i.e., it acts to facilitate a further reaction.

Applicants' response has been fully considered, however, the argument is not persuasive because the claimed method (e.g., claims 1 and 14) only recites a single method step of linking a cyclic aromatic auxiliary compound to an amine nitrogen, and there are no other steps described. Since the patent discloses the same method step of linking an aromatic carbonyl compound to an amine nitrogen as the claimed method, which meets the criteria of the claimed method.

17. Claims 1, 3, 6-8 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ehrlich *et al.* (J. Org. Chem. 61, 8831-8838 (1996)).

Ehrlich *et al.* teach the peptide H-Arg(H⁺)-Lys(Ac)-(Hmb)Ala-Val-Tyr-OH is cyclized with a high yield (double) of cyclomonomer as compared to the unmodified peptide, H-Arg(H⁺)-Lys(Ac)-Ala-Val-Tyr-OH, where Hmb (2-hydroxy-4-methoxybenzyl group) is attached to the α -

Art Unit: 1656

amino residue of Ala (scheme 1; Table 2; page 8834, right column to page 8835, left column; claims 1, 3, 6-8 and 14). Since the patent discloses the same method step of linking an aromatic carbonyl compound to an amine nitrogen as the claimed method, which meets the criteria of the claimed method.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-21, 23, 30, 31 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8-19, 32-35, 39, 40 and 46-52 of co-pending application 09/806,036. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-21, 23, 30, 31 and 35 in the instant application disclose a method of synthesis of a linear, cyclic peptide or on-resin cyclization of a peptide molecule, comprising linking a cyclic aromatic or alkyl auxiliary compound to an amine nitrogen atom. This is obvious variation in view of claims 8-19, 32-35, 39, 40 and 46-52 disclose a method of synthesis of a cyclic peptide or peptidomimetic compound of General Formula I or II, comprising preparing a linear peptide of General Formula III having A1 and A2, wherein A1 is N-substituent on the peptide backbone or a chemical moiety that

Art Unit: 1656

forces a cis conformation, and A2 is a group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide, activating the C-terminus to form a large cyclic peptide, subjecting the large cyclic peptide to ring contraction to the desired substituted cyclic peptide, and deprotecting the substituted cyclic peptide. Since both sets of claims are directed to a method of synthesis of a cyclic peptide either in solution or on a solid support, comprising preparing a linear peptide having A1 and A2 by linking a cyclic aromatic or alkyl auxiliary compound to an amine nitrogen atom, and cyclizing the peptide. Therefore, claims 1-21, 23, 30, 31 and 35 in instant application and claims 8-19, 32-35, 39, 40 and 46-52 of the co-pending application are obvious variations of a method of synthesis of a cyclic peptide either in solution or on a solid support, comprising preparing a linear peptide having A1 and A2, where A1 and A2 are used to facilitate the cyclization reaction.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



CHIH-MIN KAM
PATENT EXAMINER

CMK

July 22, 2005